Antimicrobial prophylaxis in surgery

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Objective: To provide guidelines for antimicrobial prophylaxis on the basis of the type of surgical procedure.
Options: Standard drug regimens for prophylaxis of infection in a variety of surgical procedures were considered, including a first-generation cephalosporin; an aminoglycoside in combination with metronidazole, clindamycin or erythromycin; a second-generation cephalosporin; and trimethoprim–sulfamethoxazole.
Outcomes: In order of importance: efficacy, side effects and cost.
Evidence: A MEDLINE search of articles published between January 1980 and December 1991. For clinical trial data, greatest emphasis was placed on randomized, double-blind studies using appropriate controls.
Values: The Committee on Antimicrobial Agents of the Canadian Infectious Disease Society (CIDS) and two recognized experts (T.K.W. and O.D.R.) recommended antimicrobial regimens suitable for prophylaxis of infections in surgery. Whenever possible, recommendations were based on data from randomized controlled trials.
Benefits, harms and costs: Implementation of the guidelines is expected to reduce the incidence of postoperative infections, the inappropriate use of antibiotics and costs to hospitals.
Recommendations: Antibiotic prophylaxis is recommended for operations with a high risk of postoperative wound infection or with a low risk of infection but significant consequences if infection occurs. These operations include clean–contaminated procedures and certain clean procedures. Drugs should be administered intravenously immediately before the operation. In colorectal operations oral administration also appears to be effective. A single dose is sufficient for most procedures. The regimen chosen depends on the pathogens usually associated with wound infection in a given operation, the serum half-life of the drugs, the antimicrobial susceptibility patterns in the local hospital and the cost of the drugs.
Validation: The guidelines were compared with others in standard textbooks of surgery and peer-reviewed articles. The guidelines were prepared and revised by the Committee on Antimicrobial Agents of the CIDS. They were then reviewed and revised further by the Council of the CIDS.
Sponsor: The CIDS was solely responsible for developing, funding and endorsing these guidelines.

Objectif : Fournir des lignes directrices sur la prophylaxie antimicrobienne selon le type d'intervention chirurgicale.
Options : On a examiné les schémas posologiques normaux contre l'infection dans toutes sortes d'interventions chirurgicales, y compris une céphalosporine de première génération, un

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aminoside combiné à du métronidazole, de la clindamycine ou de l'érythromycine, une céphalosporine de deuxième génération et du triméthoprime–sulfaméthoxazole.
Résultats : Par ordre d'importance : efficacité, effets secondaires et coût.
Preuves : Recherche dans MEDLINE d'articles publiés entre janvier 1980 et décembre 1991. Dans le cas des données cliniques, on a insisté davantage sur les études randomisées à double insu effectuées à l'aide des moyens de contrôle appropriés.
Valeurs : Le Comité d'agents antimicrobiens de la Société canadienne des maladies infectieuses (SCMI) et deux experts reconnus (T.K.W. et O.D.R.) ont recommandé des schémas antimicrobiens convenant au traitement d'infections dans les cas de chirurgie. Les recommandations ont été fondées dans la mesure du possible sur des données provenant d'essais contrôlés randomisés.
Avantages, préjudices et coûts : La mise en oeuvre des lignes directrices devrait réduire l'incidence d'infections postopératoires, l'utilisation indue d'antibiotiques et les coûts pour les hôpitaux.
Recommandations : On recommande une prophylaxie aux antibiotiques dans le cas des interventions qui présentent un risque élevé d'infection opératoire de la plaie ou un faible risque d'infection mais des conséquences graves en cas d'infection. Ces interventions comprennent des interventions en champ propre–contaminé et certaines interventions en champ propre. Les médicaments devraient être administrés par voie intraveineuse immédiatement avant l'intervention. Dans les cas d'interventions colorectales, l'administration par voie orale semble efficace aussi. Une dose simple suffit dans la plupart des interventions. Le schéma choisi dépend des agents pathogènes habituellement liés à l'infection de la plaie à la suite d'une intervention donnée, à la demi-vie sérique des médicaments, aux tendances à la sensibilité antimicrobienne dans l'hôpital local et au coût des médicaments.
Validation : Les lignes directrices ont été comparées à d'autres contenues dans des manuels standard de chirurgie et des articles critiqués par des pairs. Les lignes directrices ont été préparées et révisées par le Comité d'agents antimicrobiens de la SCMI et ont été examinées et révisées ensuite par le Conseil de la SCMI.
Commanditaire : La SCMI s'est chargée à elle seule de l'élaboration et du financement de ces lignes directrices auxquelles elle a donné son aval.

Postoperative wound sepsis is the most common nosocomial infection in patients undergoing surgery.[1] It is an important cause of illness, resulting in a prolongation of hospital stay, an increase in the cost of medical care and an inconvenience to patients and their families. Antibiotics have been used for prophylaxis in surgical patients with the hope of reducing the rate of postoperative wound infections. Animal studies by Burke[2] first defined the scientific basis for the perioperative use of antimicrobial agents in the prophylaxis of surgical wound infection. Clinical confirmation firmly established the efficacy of antibiotic prophylaxis in preventing wound infection.[3,4] This article provides an overview of antimicrobial prophylaxis in surgery, focusing on identification of patients at high risk of infection, principles of antibiotic administration and choice of appropriate agents.

Methods

This article was prepared in a number of stages designed to ensure an unbiased and critical approach. A recognized expert was identified by the Committee on Antimicrobial Agents of the Canadian Infectious Disease Society (CIDS) to prepare a first draft. Appropriate sources of evidence published in the medical literature between January 1980 and December 1991 were identified by a MEDLINE search. Particular attention was paid to study design, and greatest credence was given to randomized, controlled, double-blind studies. Consideration was also given to position papers, consensus statements and reviews dealing with this subject.

The first draft was reviewed by committee members, revised and reviewed again. After a second revision the article was reviewed by the Council of the CIDS. The committee chairman then made any further revisions.

Identification of patients at high risk of infection

A wound infection develops as a result of a complex interaction between the bacteria inoculated into the wound during surgery and the local and systemic resistance of the host to infection. The size of the bacterial inoculum is directly correlated with the risk of a postoperative wound infection. Surgical procedures may be classified according to the chance of the wound becoming contaminated and, by inference, to the size of the bacterial inoculum entering the wound (Table 1).[5] Increased virulence of the contaminating bacteria may also raise the likelihood of a wound infection. As well, factors such as prolonged preoperative hospital stay and the excessive use of antibiotics increase the risk of colonization with hospital-acquired pathogens. Alterations in the resistance of the host to infection may occur systemi-

cally or locally (within the wound). Systemic resistance is largely determined by characteristics of the patient and his or her disease state. Nutritional support and control of distant infection reduce the risk of wound infection. Achievement of optimal local resistance to infection is a predominantly surgical task. A variety of factors, such as the presence of blood, foreign bodies, ischemia or necrotic tissue at the operative site, may impair local host defences and increase the risk of infection. Meticulous surgical technique helps to avoid many of these contributing factors.

The primary benefit of antibiotics is reduction of the inoculum of viable bacteria in the wound. Contaminated or dirty surgical procedures are those involving an established infection; in these cases antibiotic administration should be considered therapeutic for deep infection rather than prophylactic for wound infection. The main indications for prophylactic antibiotic use in surgery are operations in which the risk of postoperative wound infection is high or in which the rate of wound infection is relatively low but the consequences of infection are significant. The use of antibiotic prophylaxis for clean–contaminated surgical procedures is widely accepted. For certain clean–contaminated operations, patients at high risk of postoperative infection can frequently be identified. For example, in a cholecystectomy the presence of acute inflammation, jaundice or common bile duct stones, or patient age of more than 70 years, is correlated with an increased rate of infected bile and consequently of wound infection.[6] Similarly, in patients undergoing gastric surgery, intragastric hypochlorhydria is associated with an increased rate of wound infection.[7] Hypochlorhydria occurs in patients with gastric outlet obstruction caused by a duodenal ulcer, those undergoing operations for gastric ulcer or carcinoma and those undergoing emergency surgery for bleeding in the upper gastrointestinal tract. In addition an obese patient undergoing a gastric bypass procedure has an increased risk of postoperative wound infection. Factors indicating higher risk of infection have been described for many general surgical, gynecologic, obstetric and urologic procedures (some of these factors for specific operations are given as footnotes in Table 2).[7–11] Knowledge of the specific risks associated with each surgical procedure helps optimize the identification of patients for antimicrobial prophylaxis.

The prophylactic use of antibiotics for clean operative procedures was originally reserved for insertion of a prosthetic device. The catastrophic results of prosthetic infection were thought to justify the small but significant reduction in the rate of infection achieved with antimicrobial use. Similarly, prophylaxis has become widely accepted in coronary artery bypass surgery because of the risk of sternal infection associated with subcutaneous wound infection. In contrast, the administration of antibiotics as prophylaxis against wound infection for most other clean operations has been considered inappropriate, as the risk of clinically important infection was perceived to be too low to justify the use of antibiotics. However, a recent study has prompted re-evaluation of this concept. Platt and associates[12] conducted a randomized, double-blind, placebo-controlled evaluation of antibiotic prophylaxis in patients undergoing breast and hernia operations to determine whether prophylaxis produced a clinically significant reduction in postoperative infections and their sequelae. Their results showed that perioperative administration of antibiotics lowered the overall infection rate, the need for postoperative antibiotic therapy and the number of nonroutine visits to physicians for wound-related problems. Wound infection rates did not differ significantly between the treatment and the control groups, although with antibiotic use there

Table 1: Classification of surgical procedures by degree of contamination and risk of subsequent infection

Type of procedure	Definition	Wound infection rate, %[5]
Clean	Atraumatic; no break in technique; gastrointestinal, genitourinary and respiratory tracts not entered	1–2
Clean–contaminated	Gastrointestinal or respiratory tract entered but without spillage; oropharynx, sterile genitourinary or biliary tract entered; minor break in technique	2–4
Contaminated	Acute inflammation; infected bile or urine; gross spillage from gastrointestinal tract	7–10
Dirty	Established infection	10–40

was a trend towards reduction of the rate. These data suggest that, for certain clean operative procedures, the prophylactic use of antibiotics may reduce perioperative illness and lower costs. Supporting studies are required to validate these conclusions.

Principles of antibiotic administration

Timing

For effective antimicrobial prophylaxis, adequate concentrations of the drug must be present in the tissues at the onset and throughout the operative procedure.[13] To achieve this goal, the initial dose should be administered parenterally immediately before the operation. Delay of the initial dose until after the operation or administration of the antibiotics too long before the procedure is associated with an increased rate of wound infection.[14–16] The second problem is particularly significant when antibiotics with a short serum half-life are used or the operative procedure is prolonged or both. In these situations a second dose should be administered during the operation to maintain effective levels of the drug in the tissues. One minor exception to these principles is noted for prophylaxis during cesarean section; in this case the initial dose is administered immediately after cord clamping.[17]

Route of administration

Intravenous administration of antibiotics is the optimal method to ensure adequate levels in tissues during most operative procedures. There is an exception to this principle for colorectal operations: preoperative oral administration of antibiotics appears to be an effective al-

Table 2: Recommended antibiotic regimens for prophylaxis during selected surgical procedures

Surgical procedure	Common microorganisms	Antibiotic regimen*
Gynecologic surgery		
Cesarean section†	Enteric gram-negative bacilli, group B streptococci, enterococci	Cefazolin (1 g IV) after cord clamping
Hysterectomy (abdominal or vaginal)	Same as cesarean section	Cefazolin (1 g IV)
Abortion		
2nd trimester	Same as cesarean section	Cefazolin (1 g IV)
1st trimester with pelvic inflammatory disease	Same as cesarean section	Cefazolin (1 g IV) or doxycycline (300 mg PO)
Orthopedic surgery		
Open reduction or internal fixation of fracture	*Staphylococcus aureus*, *Staphylococcus epidermidis*, enteric gram-negative bacilli in complex infection	Cefazolin (1 g IV); add gentamicin (1.5 mg/kg) if infection is complex
Joint replacement	*S. aureus*, *S. epidermidis*	Cefazolin (1 g IV)
Laminectomy and spinal fusion	*S. aureus*, *S. epidermidis*	No proven benefit of prophylaxis
Lower extremity amputation for ischemia	Enteric gram-negative bacilli, anaerobic bacteria	Cefoxitin (2 g IV)
General surgery		
Gastric resection or percutaneous gastrostomy	Enteric gram-negative bacilli, gram-positive cocci (especially enterococci), *Bacteroides* species occasionally	Cefazolin (1 g IV)
Biliary tract surgery‡	Enteric gram-negative bacilli, enterococci, clostridia	Cefazolin (1 g IV)
Colon surgery	Enteric gram-negative bacilli, anaerobic bacteria (especially *Bacteroides fragilis*)	Neomycin and erythromycin (PO), or gentamicin (1.5 mg/kg) plus metronidazole (500 mg) or clindamycin (300 mg), or cefoxitin (2 g IV), or cefotetan (2 g IV)
Appendectomy (nonperforated)	Enteric gram-negative bacilli, anaerobic bacteria (especially *B. fragilis*)	Gentamicin (1.5 mg/kg) plus metronidazole (500 mg) or clindamycin (300 mg), or cefoxitin (2 g IV), or cefotetan (2 g IV)
Hernia repair	*S. aureus*, *S. epidermidis*	Cefazolin (1 g IV)

*IV = intravenously, PO = orally.
†Antibiotic prophylaxis is indicated for high-risk procedures, including unscheduled cesarean section after active labour and after premature rupture of membranes.
‡Prophylaxis is indicated in patients over 70 years of age or those with acute cholecystitis, jaundice or common bile duct stones.

ternative to intravenous administration in preventing wound infections in this type of surgery.[18] Antibiotics administered orally prevent infection by reducing the high colonic bacterial inoculum rather than by achieving high concentrations in the wound.

Duration

A single dose of antibiotics before the operation is sufficient prophylaxis for most surgical procedures.[19] This principle is well established for biliary-tract, gastric and colonic surgery, vaginal hysterectomy and transurethral prostatectomy. In many studies comparing single-dose with multidose regimens there was no difference in rates of postoperative wound infection between study and control groups.[20]

For some surgical procedures, the number of doses of antimicrobials required for optimal prophylaxis has not been precisely defined. For example, in coronary artery bypass surgery, results from a few published studies support the use of single-dose antimicrobial prophylaxis.[21,22] However, these studies generally compared an antibiotic with a long half-life, such as ceftriaxone, and traditional regimens of 24 to 48 hours using cefazolin. The high cost of advanced-generation cephalosporins offsets the potential savings associated with single-dose administration. It is not clear whether a single dose of cefazolin is sufficient prophylaxis for these procedures.

Some researchers have suggested that prolonged prophylactic use of antibiotics is appropriate when drains or catheters remain in situ for several days after the operation. The antibiotics would presumably protect the wound from a secondary infection that originated in the foreign body and reached the wound by a hematoge-

Table 2: continued

Surgical procedure	Common microorganisms	Antibiotic regimen*
Head and neck surgery		
Oropharyngeal surgery§	Viridans streptococci, *S. aureus*, enteric gram-negative bacilli, oral anaerobic bacteria (such as peptostreptococci and fusobacteria)	Gentamicin (1.5 mg/kg) and clindamycin (600 mg), or cefazolin (1 g IV)
Thoracic surgery		
Pulmonary resection (lobectomy and pneumonectomy)	Staphylococci, *Streptococcus pneumoniae*, enteric gram-negative bacilli, oral anaerobic bacteria	Cefazolin (1 g IV)
Vascular surgery		
Procedures with or without prosthetic graft	*S. aureus*, *S. epidermidis* streptococci, enteric gram-negative bacilli	Cefazolin (1 g IV)
Cardiac surgery		
Valve and coronary artery bypass surgery	*S. aureus*, *S. epidermidis*, enteric gram-negative bacilli	Cefazolin (1 g IV), or cefamandole (2 g IV), or cefuroxime (1.5 g IV)
Pacemaker insertion	*S. aureus*, *S. epidermidis*	Prophylaxis is not indicated
Urologic surgery		
Prostate surgery‖	*Escherichia coli*, *Klebsiella* species, enterococci, *Pseudomonas* species	Cefazolin (1 g IV)
Urethral dilatation		Prophylaxis is not indicated
Neurosurgery		
Craniotomy¶	*S. aureus*	Clindamycin (600 mg IV), or vancomycin (1 g IV) plus gentamicin (1.5 mg/kg IV)
Cerebrospinal fluid shunting operations**	*S. aureus*	Trimethoprim (160 mg IV) plus sulfamethoxazole (800 mg IV)

§Prophylaxis is indicated in major surgical procedures involving an incision through oral or pharyngeal mucosa; it is not indicated for tonsillectomy, adenoidectomy or rhinoplasty.
‖Antibiotics are beneficial if the urine is infected before the operation. Prophylaxis may be indicated in patients with sterile urine as well, depending on the rate of infection in the local hospital.
¶Prophylaxis is indicated in patients at high risk of infection (e.g., those undergoing repeat exploratory surgery or microsurgery).
**Prophylaxis is indicated if the rate of infection in the hospital is greater than 10% to 20%.

nous route.[23] However, results of studies of single-dose and 24-hour regimens appear to invalidate this concept. For operations in which single-dose antimicrobial prophylaxis is not established, future studies should help define its role.

Choice of antibiotic regimen

There are several considerations when selecting an antimicrobial regimen for prophylaxis. The most important principle is that the antibiotics selected should be effective against the pathogens most frequently responsible for wound infection after the particular operation. However, they need not be active against every microorganism in the initial bacterial inoculum, since some organisms may not contribute to wound infection. Other issues worth considering are the serum half-life of each drug, the local hospital antimicrobial susceptibility patterns and the cost of each drug. Table 2 shows several common operations, the microbial isolates most often recovered from wound infections associated with each and the recommended antibiotic selection.[24,25] Clinical studies evaluating the efficacy of various antimicrobial agents for prophylaxis in surgery are published each year; however, many of these are flawed by errors in experimental design. We urge clinicians to consider whether a trial has been adequately designed before accepting the investigator's conclusions. The important criteria for design and reporting of the results of such a trial are the following.

- It is prospective, randomized and, ideally, double-blind.
- Inclusion and exclusion criteria are defined.
- It includes written definitions of wound infection and other outcome measures.
- Risk factors of the hosts are comparable in all arms of the study.
- The operative procedures are well defined and distributed equally in all arms of the study.
- The choice of antibiotic is appropriate for the expected pathogens and their antimicrobial susceptibilities.
- The antibiotic dosage is correct.
- Concomitant use of other perioperative antibiotics and antiseptics is controlled.
- The antibiotics used have minimal toxic effects.
- There is a sufficient sample size to demonstrate that significant differences between antibiotic regimens exist or do not exist.

Side effects

Side effects of appropriate antimicrobial prophylaxis are rare. The main ones are allergic reactions and antibiotic-associated colitis. An increased sensitivity to warfarin has been described in patients receiving cefamandole prophylaxis for prosthetic valve surgery.[26] Prolonged use of antibiotics is associated with an increased risk of drug toxicity, a change in the antimicrobial susceptibility pattern of pathogens and an alteration in the patient's gastrointestinal flora.[27]

Inappropriate prophylactic use of antibiotics

The guidelines given here are widely recognized as being appropriate to reduce wound infection rates and minimize side effects of antimicrobial therapy. However, inappropriate prophylactic use of antimicrobials is common. Frequent errors include incorrect timing of the first dose, extension of prophylaxis beyond 24 hours, incorrect selection of an antibiotic and inappropriate dosage regimens. Techniques for the optimal usage of antibiotics have been described.[28]

Conclusions

Antimicrobial prophylaxis for the prevention of wound infection is well founded on experimental evidence and clearly established in clinical practice. The indications for use and characteristics of patients at high risk of infection have been defined. Antibiotics should be administered intravenously before the operation to ensure adequate levels in tissues throughout the surgical procedure. In colorectal operations oral antimicrobial regimens are an alternative measure to decrease the number of bacteria to which the wound is exposed. In general, therapy should last less than 24 hours and, under some circumstances, may consist of a single dose. The antibiotic regimen should be chosen on the basis of the expected infecting pathogens at the surgical site and the local susceptibility patterns of these microorganisms. Appropriate use of antibiotics reduces wound infection rates, thereby preventing illness in patients and lowering costs to hospitals.

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